

## **REMARKS/ARGUMENTS**

### **Description Amendments**

By the present amendment, the description on page 11, line 15, has been amended to insert a sequence identifier for the protein depicted in Figure 1.

The description on page 15, line 30, has been amended to delete the website hyperlink.

The Applicants submit that no new matter has been added to the description as a result of these amendments and entry of the description amendments is respectfully requested.

### **Sequence Listing Amendments**

By the present amendment, the sequence listing has been amended to include the sequence for the dopamine D1 receptor modified with a nuclear translocation sequence (NLS) as SEQ ID NO:159. Support for this amendment is found in Figure 1 of the application as filed. Further, page 1 was amended to insert our reference number at <130> and to correct the number of sequences at <160>.

The Applicants submit that no new matter has been added to the sequence listing as a result of this amendment and entry of the sequence listing amendment is respectfully requested.

In order to comply with the requirements of 37 C.F.R. 1.825, Applicants are also submitting herewith a substitute Sequence Listing in computer readable form including all previously submitted data with the amendment incorporated therein, accompanied by a statement, set forth below, that the copy in computer readable form is the same as the substitute copy of the "Sequence Listing.

In accordance with the requirements of 37 C.F.R. 1.825 the undersigned verifies that then substitute paper form of the Sequence Listing and the computer readable form of the Sequence Listing are the same. No new matter has been added.

### **Claim Amendments**

By the present amendment, claims 1 and 37 have been amended to incorporate the subject matter of claims 5 and 40, respectively. Accordingly, claims 5 and 40 have been canceled without prejudice.

Claim 16 has been amended so that it depends on claim 2 to correct a clerical error.

Claims 8 and 43 have been amended to remove the term "optionally". Claim 11 has been amended to replace the term "optionally" with traditional Markush terminology.

Claims 6 and 41 have been amended to depend on claims 1 and 37, respectively.

Claims 19, 20, 48 and 49 have been amended to insert the term "a" or "an" (as appropriate) preceding each receptor subtype as requested by the Examiner.

Claims 20 and 49 have been amended to replace the term "or" with the term ", and" between the expressions "insulin receptor" and "a low density lipoprotein receptor" to utilize proper the Markush format.

Claims 4, 19, 61-62, 64-66, 68, 73-77, 84, 87, 90-93, 96-97, 99-101, 103, 106, 112-115 and 122 have been canceled without prejudice.

Claims 1, 2, 6, 8, 11, 16-20, 27, 30-31, 34, 37, 38, 41, 43, 46-49, 56 and 59 are pending in the present application.

The claim amendments have been made without prejudice and without acquiescing to any of the Examiner's objections. The Applicants reserve the right to file any of the cancelled subject matter in a divisional patent application. The Applicants submit that no new matter has been entered by the present amendment and entry of the claim amendments is respectfully requested.

The Office Action dated November 30, 2006 has been carefully considered. It is believed that the claims submitted herewith and the following comments represent a complete response to the Examiner's comments and place the present application in condition for allowance. Reconsideration is respectfully requested.

#### **Restriction Requirement**

The Examiner notes that claims 37-41, 43, 46-49, 56 and 59 are withdrawn as being drawn to a non-elected invention. The Applicants timely traversed this restriction requirement in their reply filed on June 22, 2006. The Examiner found the Applicants arguments to not be persuasive because he contends that a method employing a transfected cell expressing a heterologous transmembrane protein comprising an NLS wherein distribution of the protein is determined, is not an inventive concept that may be used to link the inventions of Group 1 (claims 1, 2, 6, 8, 11, 16-20, 27, 30-31 and 34) and Group 2 (claims 37, 38, 41, 43, 46-49, 56 and 59) because the Examiner alleges that this concept is taught by Conway et al. (J. Cellul. Phys. 189:341-355, 2001, hereinafter "Conway") and Chen et al. (Am. J. Physical. Renal. Physiol. 279:F440-F-448, 2000, hereinafter "Chen"). The Examiner further states that if the elected claims be amended to recite a method that employs a distinguishing product, the Applicants are entitled to the present claims of Group 2 if those claims require that distinguishing product.

While not agreeing with the Examiner, to expedite the allowance of this case, the Applicants have, by the present amendment, amended claims 1 and 37 to incorporate the subject matter of claims 5 and 40, respectively. The Examiner admits in the Action of November 30, 2006, that the subject matter of claims 5 and 40 are distinguished from

Conway and Chen, accordingly, the Applicants request that claim 37, as amended herein, as well as claims 38, 41, 43, 46-49, 56 and 59, dependent thereon, be rejoined in the present application.

#### **Objection to the Description**

The Examiner has objected to the description for containing an embedded hyperlink on page 15, line 30. The Applicants have amended the description to remove the hyperlink found on page 15, which is to the website "Genbank", the location of which would be well known to a person skilled in the art.

In light of this amendment, the Applicants request that the Examiner's objection to the description be withdrawn.

#### **Objection to the Figures**

The Examiner has objected to the figures under 37 CFR §1.821(d) for not containing a proper sequence identifier for the amino acid sequence presented in Figure 1. The Applicants have amended the Sequence listing to include the protein sequence found in Figure 1 as SEQ ID NO: 159 and page 11, at line 15, has been amended to include a reference to this sequence identifier in the Brief Description of the Drawings, which, according to MPEP 2422.02, fulfills the requirements of 37 CFR §1.821(d).

In light of the above amendments, the Applicants request that the Examiner's objection to the Figures be withdrawn.

#### **35 USC §112, First Paragraph**

The Examiner has objected to claims 1, 2, 4-6, 8, 11, 17-20, 27, 30, 31 and 34 under 35 USC §112, first paragraph, as failing to comply with the enablement requirement. Specifically, the Examiner contends that a person skilled in the art would have no reason to believe that the incorporation of an NLS into a transmembrane protein will have any effect on the localization of that protein into a prokaryotic cell upon exposure of the protein to a compound that interacts with that protein, since a

prokaryotic cell, by definition, does not have a nucleus. The Applicants respectfully disagree with the Examiner for the reasons that follow.

As taught on page 8, lines 7-16, of the application as filed, the NLS motifs are recognized and bound by the importin  $\alpha$ - $\beta$  receptor complex. The importin  $\alpha$ - $\beta$  receptor complex is a cytosolic protein and binding of this protein with the NLS results in transportation of the bound NLS-containing protein to the nuclear core. The Applicants submit that a person skilled in the art would understand that, the binding of a NLS motif by an importin  $\alpha$ - $\beta$  receptor complex may not be dependent on the presence of a nucleus in the cell. Since the importin  $\alpha$ - $\beta$  receptor complex is located in the cytosol of a cell, the binding of a transmembrane protein comprising an NLS to this complex may be expected to alter the distribution of that protein from the membrane simply into the cytosol of the cell of a prokaryote. This altered distribution, as well as any effect on this distribution by the presence of a candidate compound, may be detected using the methods of the present invention. Accordingly, the Applicants submit that the method of the present invention as claimed in claims 1, 2, 4-6, 8, 11, 17-20, 27, 30, 31 and 34 is enabled and meets the requirements of 35 USC §112, first paragraph.

In light of the above, the Applicants request that the Examiner's objection to claims 1, 2, 4-6, 8, 11, 17-20, 27, 30, 31 and 34 under 35 USC §112, first paragraph, be withdrawn.

Claim 16 has been objected to under 35 USC §112, first paragraph, because it depends on a canceled claim. By the present amendment, claim 16 has been amended so that it depends on claim 2.

In light of the above, the Applicants request that the Examiner's objection to claim 16 under 35 USC §112, first paragraph, be withdrawn.

### **35 USC §112, Second Paragraph**

The Examiner has objected to claims 8 and 11 under 35 USC §112, Second Paragraph, alleging that the term “optionally” renders these claims indefinite. Claim 8 has been amended to remove the term “optionally” and claim 11 has been amended to replace the term “optionally” with traditional Markush wording.

In light of the above, the Applicants request that the Examiner’s objection to claims 8 and 11 under 35 USC §112, second paragraph, be withdrawn.

Claim 16 has been objected to under 35 USC §112, second paragraph, because it depends on a canceled claim. By the present amendment, claim 16 has been amended so that it depends on claim 2.

In light of the above, the Applicants request that the Examiner’s objection to claim 16 under 35 USC §112, second paragraph, be withdrawn.

The Examiner has objected to claims 19 and 20 under 35 USC §112, second paragraph, and requested that the Applicants amend these claims to refer to “a dopamine D1 receptor”, “a dopamine D2 receptor”, etc. The Applicants have made this amendment.

In light of the above, the Applicants request that the Examiner’s objection to claims 19 and 30 under 35 USC §112, second paragraph, be withdrawn.

### **35 USC §102(a)**

The Examiner has objected to claims 1, 2, 4, 8, 17, 18, 30, 31 and 34 under 35 USC §102(a) as being anticipated by Conway. While not agreeing with the Examiner, to expedite the allowance of this case, the Applicants have amended claim 1 to include the subject matter of claim 5, which renders the Examiner’s objection moot.

In light of the above, the Applicants request that the Examiner's objection to claims 1, 2, 4, 8, 17, 18, 30, 31 and 34 under 35 USC §102(a) be withdrawn.

**35 USC §102(b)**

The Examiner has objected to claims 1, 2, 4, 8, 17, 18, 30, 31 and 34 under 35 USC §102(a) as being anticipated by Chen. While not agreeing with the Examiner, to expedite the allowance of this case, the Applicants have amended claim 1 to include the subject matter of claim 5, which renders the Examiner's objection moot.

In light of the above, the Applicants request that the Examiner's objection to claims 1, 2, 4, 8, 17, 18, 30, 31 and 34 under 35 USC §102(a) be withdrawn.

Early and favorable action on the merits is awaited. Should the Examiner deem it beneficial to discuss the application in greater detail, the Examiner is invited to contact the undersigned by telephone at (416) 957-1683 at the Examiner's convenience.

The Commissioner is hereby authorized to charge any deficiency in fees (including any claim fees) or credit any overpayment to Deposit Account No. 02-2095.

Respectfully submitted,

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Enclosures:  
Sequence Listing – paper form – page 1 to 40; and  
Sequence Listing – Computer Readable Form.